CLAIMS

We claim:

1. A method for determining whether an agent can be used to reduce the proliferation and /or cause the death of cancer cells or inhibit the growth of a cancer cell population, comprising the steps of: a) obtaining a sample of cancer cells; b) determining and quantifying the level of expression in the cancer cells of a marker identified in Tables 1 and 5; and c) identifying that an agent can be used to reduce the proliferation and/or cause the death of said cancer cells when the marker is expressed at a certain level.

2. The method of claim 1, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a transcribed polynucleotide or portion thereof, wherein the transcribed polynucleotide comprises the marker.

3. The method of claim 2, wherein the transcribed polynucleotide is an mRNA or siRNA.

4. A method of claim 2, wherein the transcribed polynucleotide is cDNA.

5. The method of claim 1, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a protein or protein fragment corresponding to the marker.

6. The method of claim 2, wherein the step of detecting further comprises amplifying the transcribed polynucleotide using RT-PCR.

7. The method of claim 6, wherein the step of detecting the level of expression includes:

initially screening a plurality of genes representing different functional classes,

evaluating an expanded group of genes represented by genes that are positively or negatively associated in the initial screening,

comparing the expression of the positively and negatively associated genes to form at least one interactive gene expression index (IGEI),

using individual gene analysis and IGEI analysis, and

developing at least one model of the level that describes an association between the level of detection of the expression of at least one of the markers identified in Tables 1 and 5 and reduced proliferation and/or increased death.

8. The method of claim 5, wherein the presence of the protein or protein fragment is detected using a reagent which specifically binds with the protein or protein fragment.

9. The method of claim 8, wherein the reagent is selected from the group consisting of an antibody, an antibody derivative, and an antibody fragment.

10. The method of claim 1, wherein the cancer cells are selected from the group consisting of cancer cell lines and cancer cells obtained from a patient.

11. The method of claim 1, wherein the agent is a chemotherapeutic compound.

12. The method of claim 11, wherein the agent is a platinum compound.

13. The method of claim 12, wherein the agent is cisplatin.

14. A method for determining whether an agent is effective in treating cancer, comprising the steps of: a) obtaining a sample of cancer cells; b) exposing the sample to an agent; c) determining and quantifying the level of expression of a marker identified in Tables 1 and 5 in the sample exposed to the agent and in a sample that is not exposed to the agent; and d) identifying that an agent is effective in treating cancer when expression of the marker is altered in the presence of said agent.

15. The method of claim 14, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a transcribed polynucleotide or portion thereof, wherein the transcribed polynucleotide comprises the marker.

16. The method of claim 15, wherein the transcribed polynucleotide is an mRNA or siRNA.

17. A method of claim 15, wherein the transcribed polynucleotide is cDNA.

18. The method of claim 14, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a protein or protein fragment corresponding to the marker.

19. The method of claim 15, wherein the step of detecting further comprises amplifying the transcribed polynucleotide using RT-PCR.

20. The method of claim 19, wherein the step of detecting the level of expression includes:

initially screening a plurality of genes representing different functional classes,

evaluating an expanded group of genes represented by genes that are positively associated in the initial screening,

comparing the expression of the positively or negatively associated genes to form at least one interactive gene expression index (IGEI),

using the IGEI analysis, and

developing at least one model that describes an association between the level of detection of the expression of at least one of the markers identified in Tables 1 and 5 and reduced proliferation and/or cell death.

21. The method of claim 19, wherein the presence of the protein or protein fragment is detected using a reagent which specifically binds with the protein or protein fragment.

22. The method of claim 21, wherein the reagent is selected from the group consisting of an antibody, an antibody derivative, and an antibody fragment.

23. The method of claim 14, wherein the cancer cells are selected from the group consisting of cancer cell lines and cancer cells obtained from a patient.

24. The method of claim 14, wherein the agent is a chemotherapeutic compound.

25. The method of claim 24, wherein the agent is a platinum compound.

26. The method of claim 26, wherein the agent is cisplatin.

27. A method for determining whether treatment with an agent should be continued in a cancer patient, comprising the steps of: a) obtaining two or more samples comprising cancer cells from a patient during the course of treatment with the agent; b) determining and quantifying the level of expression of a marker identified in Tables 1 and 5 in the two or more samples; and c) continuing treatment when the expression level of the marker is not significantly altered during the course of treatment.

28. The method of claim 27, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a transcribed polynucleotide or portion thereof, wherein the transcribed polynucleotide comprises the marker.

29. The method of claim 28, wherein the transcribed polynucleotide is an mRNA or siRNA.

30. A method of claim 28, wherein the transcribed polynucleotide is cDNA.

31. The method of claim 27, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a protein or protein fragment corresponding to the marker.

32. The method of claim 28, wherein the step of detecting further comprises amplifying the transcribed polynucleotide using RT-PCR.

33. The method of claim 32, wherein the step of detecting the level of expression includes:

initially screening a plurality of genes representing different functional classes,

evaluating an expanded group of genes represented by genes that are positively or negatively associated in the initial screening,

comparing the expression of the positively and negatively associated genes to form at least one interactive gene expression index (IGEI),

using the IGEI analysis, and

developing at least one model that describes an association between the level of detection of the expression of at least one of the markers identified in Tables 1 and 5 and reduced proliferation and/or cell death.

34. The method of claim 31, wherein the presence of the protein or protein fragment is detected using a reagent which specifically binds with the protein or protein fragment.

35. The method of claim 34, wherein the reagent is selected from the group consisting of an antibody, an antibody derivative, and an antibody fragment.

36. The method of claim 27, wherein the cancer cells are selected from the group consisting of cancer cell lines and cancer cells obtained from a patient.

37. The method of claim 29, wherein the agent is a chemotherapeutic compound.

38. The method of claim 38, wherein the agent is a platinum compound.

39. The method of claim 38, wherein the agent is cisplatin.

40. A method for identifying new cancer treatments, comprising the steps of: a) obtaining a sample of cancer cells; b) determining and quantifying the level of expression of a marker identified in Tables 1 and 5; c) exposing the sample to the cancer treatment; d) determining the level of expression of the marker in the sample exposed to the cancer treatment; and e) identifying that the cancer treatment is effective in treating cancer when the marker is expressed at a certain level.

41. The method of claim 40, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a transcribed polynucleotide or portion thereof, wherein the transcribed polynucleotide comprises the marker.

42. The method of claim 41, wherein the transcribed polynucleotide is an mRNA or siRNA.

43. A method of claim 41, wherein the transcribed polynucleotide is cDNA.

44. The method of claim 40, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a protein or protein fragment corresponding to the marker.

45. The method of claim 40, wherein the step of detecting further comprises amplifying the transcribed polynucleotide using RT-PCR.

46. The method of claim 45, wherein the step of detecting the level of expression includes:

initially screening a plurality of genes representing different functional classes,

evaluating an expanded group of genes represented by genes that are positively or negatively associated in the initial screening,

comparing the expression of the positively and negatively associated genes to form at least one interactive gene expression index (IGEI),

using the IGEI analysis, and

developing at least one model that describes an association between the level of detection of the expression of at least one of the markers identified in Tables 1 and 5 and reduced proliferation and/or cell death.

47. The method of claim 44, wherein the presence of the protein or protein fragment is detected using a reagent which specifically binds with the protein or protein fragment.

48. The method of claim 47, wherein the reagent is selected from the group consisting of an antibody, an antibody derivative, and an antibody fragment.

49. The method of claim 40, wherein the cancer cells are selected from the group consisting of cancer cell lines and cancer cells obtained from a patient.

50. The method of claim 40, wherein the agent is a chemotherapeutic compound.

51. The method of claim 50, wherein the agent is a platinum compound.

52. The method of claim 51, wherein the agent is cisplatin.

53. A method of diagnosing non small cell lung cancer in a patient, comprising: (a) detecting and quantifying the level of expression in a tissue sample of c-myc, E2F-1 and p21 genes; wherein differential expression of the c-myc, E2F-1 and p21 genes is indicative of non small cell lung cancer.

54. A method of detecting the progression of non small cell lung cancer in a patient, comprising: (a) detecting and quantifying the level of expression in a tissue sample of two or more c-myc, E2F-1 and p21 genes; wherein differential expression of the c-myc, E2F-1 and p21 genes is indicative of non small cell lung cancer progression.

55. A method of monitoring the treatment of a patient with non small cell lung cancer, comprising: (a) administering a pharmaceutical

composition to the patient; (b) preparing a gene expression profile from a cell or tissue sample from the patient; and (c) comparing the patient gene expression profile to a gene expression from a cell population selected from the group consisting of normal lung cells, and non small cell lung cancer.

56. A method of treating a patient with non small cell lung cancer, comprising: (a) administering to the patient a pharmaceutical composition, wherein the composition alters the expression of at least one gene in Tables 1 and 5 or c-myc, E2F-1 and p21 genes; (b) preparing an IGEI comprising standardized gene expression values using StaRT-PCR from a cell or tissue sample comprising tumor cells obtained before treatment and another sample obtained after treatment; and (c) comparing the sample obtained prior to treatment with the sample obtained after treatment.

57. A method of screening for an agent capable of modulating the onset or progression of non small cell lung cancer, comprising: (a) preparing a first IGEI comprising standardized gene expression values using StaRT-PCR of a cell population comprising non small cell cancer cells, wherein the first IGEI determines the expression level of one or more genes from Tables 1 and 5 or c-myc, E2F-2 and p21 genes; (b) exposing the cell population to the agent; (c) preparing second IGEI comprising standardized gene expression values using StaRT-PCR of the agent-exposed cell population; and (d) comparing the first and second IGEIs.

58. A solid phase hybridization template for measuring, in a standardized fashion, PCR products following standardized quantitative RT-PCR comprising:

a) preparing at least one solid phase hybridization template where, for each gene, an oligonucleotide of any length that will bind with specificity to both the competitive template, CT, and native template, NT, is spotted to a filter;

b) identifying a suitable oligonucleotide such that the region between the forward primer (common to both the NT and CT) and the 3' 20 bp of the reverse CT primer is evaluated;

c) attaching an oligonucleotide to a solid support at a previously designated location;

d) amplifying the CT and NT PCR products and hybridizing to the spots of the filter wherein each gene (NT and CT) are amplified separately;

e) pooling the PCR products for hybridization;

f) preparing two oligonucleotide probes, each labeled with a different fluor, for each gene wherein one oligonucleotide is homologous to, and will bind to sequences unique to the NT for a gene that was PCR-amplified such that this oligonucleotide binds to the region of the NT that is not homologous to the CT and is labeled with a different fluor, and wherein the other oligonucleotide is specific to the CT and is labeled with a different fluor such that this other oligonucleotide is homologous to and will bind to CT sequences that span the 3' end of the reverse primer.

59. The solid phase hybridization template of claim 58 wherein the NT-specific and CT-specific oligonucleotides for multiple genes are mixed in equal amounts and hybridized to the gene-specific PCR products bound to the gene-specific oligonucleotides spotted on the filter.

60. The solid phase hybridization template of claim 59 wherein the ratio between the fluors bound to the spot quantifies the NT relative to CT.

61. The solid phase hybridization template of claim 60, wherein, although there may be different binding affinities between the CT and CT probe relative to that between the NT and NT probe, this difference is consistent between different samples assessed, and from one experiment to another.

62. The solid phase hybridization template of claim 58 wherein the template comprises at least one standardized microarray, microbeads, glass slides, or chips prepared by photolithography.

63. The solid phase hybridization template of claim 60, wherein the solid support comprises at least one of a membrane, a glass support, a filter, a tissue culture dish, a polymeric material, a bead and a silica support.

64. The solid phase hybridization template of claim 63,wherein the solid support comprising at least two oligonucleotides, wherein each of the oligonucleotides comprises a sequence that specifically hybridizes to at least one gene in Tables 1 and 5 or the c-myc, E2F-1 and p21 genes.

65. The solid phase hybridization template of claim 64, wherein the oligonucleotides are covalently attached to the solid support.

66. The solid phase hybridization template of claim 64, wherein the oligonucleotides are non-covalently attached to the solid support.

67. A computer system comprising: (a) a database containing information identifying the standardized numerical expression level in

units of molecules/10^6 β-actin molecules in lung tissue of a set of genes comprising at least two genes in Tables 1 and 5 or c0myc, E2F-1 and p21 genes; and (b) a user interface to view the information.

68. A computer system of claim 67, wherein the database further comprises sequence information for the genes.

69. A computer system of claim 67, wherein the database further comprises information identifying the standardized numerical expression level in units of molecules/10^6 β-actin molecules for the set of genes in normal lung tissue.

70. A computer system of claim 67, wherein the database further comprises information identifying the standardized numerical expression level in units of molecules/10^6 β-actin molecules of the set of genes in non small cell cancer tissue.

71. A computer system of any of claims 67-70, further comprising records including descriptive information from an external database, which information correlates said genes to records in the external database.

72. A computer system of claim 71, wherein the external database is Genbank.

73. A method of using a computer system of any one of claims 67-72 to present information identifying the standardized numerical expression level in a tissue or cell of at least one gene in Tables 1 and 5 and c-myc, E2F-1 and p21 genes, comprising: (a) comparing the standardized numerical expression level of at least one gene in Tables 1

and 5 or c-myc, E2F-1 and p21 genes in the tissue or cell to the level of expression of the gene in the database.

74. A method of claim 73, wherein the expression level of at least two genes are compared.

75. A method of claim 73, wherein the expression level of at least five genes are compared.

76. A method of claim 73, wherein the expression level of at least ten genes are compared.

77. A method of claim 73, further comprising displaying the level of expression of at least one gene in the tissue or cell sample compared to the expression level in lung cancer or in normal lung tissue.

78. A kit comprising at least one solid support of any one of claims 64-66 packaged with gene expression information for said genes.

79. A kit of claim 78, wherein the gene expression information comprises gene expression levels in a tissue or cell sample exposed to a toxin.

80. A kit of claim 79, wherein the gene expression information is in an electronic format.